REVIEW

Postoperative pain management following ambulatory anesthesia: challenges and solutions

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Keywords: ambulatory surgery, short-stay surgery, multimodal analgesia, nonopioids, local anesthetics, regional anesthesia

Introduction

There is a worldwide and ever-increasing trend toward performance of surgery in day- or short-stay settings as so-called ambulatory surgery. This progress has resulted in increasingly complex and major surgery being performed in this setting, partially driven by global economic pressures on our health care systems.¹ As a consequence of this development, more and more complex procedures are performed in older, almost geriatric, or chronically impaired patients including more with ASA (American Society of Anesthesiologists) 3 status than ever before.

This means also that more patients after potentially more painful procedures are going home within 24 hours of surgery than ever before. Lack of adequate postoperative pain management becomes one important limiting factor on which operations can be performed in an ambulatory setting; another one may be the adverse effects of more aggressive analgesia, eg, postoperative nausea and vomiting (PONV) increasing with increasing opioid requirements leading to increased rates of readmission.

Ambulatory Anesthesia 2015:2 11-20

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http://dx.doi.org/10.2147/AA.S54869

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This review addresses the challenges posed by these relatively new scenarios and show some of the solutions that have been developed.

Quality of pain relief after ambulatory surgery

A considerable number of studies have looked at the quality of analgesia in the ambulatory surgery setting, and overall the results are rather disappointing and disenchanting.

Pain after discharge remains the most common complication after ambulatory surgery. This has been shown only a few years ago in two large Swedish surveys, as well as in a general² pediatric population.³ Similar findings were reported in selected populations, eg, after urological surgery in Spain.⁴ A prospective study after day-case laparoscopic cholecystectomy identified that, after 24 hours, 65% of patients reported moderate and 23% severe pain.⁵ Even after operations usually considered as not very painful, such as laparoscopic gynecological surgery, only 60% of the patients were satisfied with their pain relief.⁶ And these disappointing data continue through to cataract day-stay surgery, where 10% of patients reported ocular pain at 24 hours, 9% at 7 days, and 7% at 6 weeks.⁷

As already alluded to above, these results are not limited to adults but also mirrored in pediatric studies. Here, ear–nose–throat (ENT) procedures have been looked at in detail; eg, after adenotonsillectomy, 52% of children had a pain score >5/10 on day 3 and 30% on day 7.⁸ It is of note here that in a comparison of day-stay versus overnight inpatient stay, pain scores during the first 24 hours were only slightly increased for day-stay patients, and that the maximum pain scores at 24 hours and 7 days were similar.⁹ This is contradicted by another audit, which found pain reports to be significantly higher at home than in the hospital.¹⁰ Pain relief needs to also be provided for an extended period of time at home; the majority of children after tonsillectomy required at least one analgesic medication for 7 days after surgery.¹¹

Adverse effects of pain after ambulatory surgery

Poor analgesia after any surgery is unacceptable and distressing to patients. This is even more so in an ambulatory setting, where patients have limited access to health care providers and analgesic medications. As a consequence, they may feel abandoned. Callbacks to the surgical center and/or family practitioners and/or emergency departments and readmissions are the result; the most common reason for unplanned hospital admission after ambulatory surgery is unrelieved pain.^{12,13} Poor analgesia at home may lead to sleep disturbance and limited early mobilization, thereby impairing early return to normal function and work.¹⁴

Last, but not least, exposure to severe pain can cause adverse long-term effects in adults as well as in children.¹⁵ Up to 50% of adults develop chronic pain subsequent to surgery and trauma, with severity of acute pain a major predictive factor;¹⁶ similar effects have been reported in children.¹⁷

But the consequences of inadequate analgesia begin much earlier after the operation when this issue delays patient discharge; here again, pain was the most common cause of delayed recovery (24% of patients).¹⁸ While opioids can cause nausea and vomiting, uncontrolled pain is also a major cause, often leading to extended stay in the recovery room.^{19,20}

All these adverse effects of unrelieved pain have not only human consequences but also economic ones because delays in discharge and readmissions are costly.²¹ Finally, the medicolegal consequences of poor analgesia need to be recognized.²²

Therefore, the challenge of provision of analgesia after ambulatory surgery needs to be accepted and solutions need to be found.

Reasons for poor analgesia after ambulatory surgery

The failures to provide sufficient analgesia described above occur despite a wide body of evidence for the best approaches to management of acute pain and despite the clinical availability of a wide range of excellent analgesic drugs.²³ One potential cause for the lack of improvement in this area has been identified by German surveys as poor adherence to such guidelines for acute pain therapy.^{24,25} This phenomenon has been described as being due to the "disconnect" between the significant scientific advances in the area of multimodal analgesia and the lack of implementation of these concepts into routine clinical practice, in an editorial by White.²⁶ This editorial highlights a number of relevant issues in this setting, such as the extensive reliance on opioids leading to complications and the lack of continuation of analgesic therapies into the post-discharge period.

However, improving things is not always easy, as extensively shown in the pediatric literature. Here, barriers against good analgesia have been identified as parental, child, medication, and system factors.²⁷ However, overcoming these barriers is not easy because differences in parental attitudes, understanding and access to medications, nausea, or fear of side effects are relevant contributing factors. Attempts to address such problems by supplying a discharge medication

package²⁸ or telephone follow-up by nurses failed after ambulatory tonsillectomy.²⁹

General strategies to improve analgesia

In view of the above shortcomings, and to address current deficits in the management of acute pain after ambulatory surgery, a most recent review has suggested a practical three-step approach.³⁰ The suggested steps are 1) identification of highrisk patients, 2) implementation of multimodal analgesic strategies, and 3) ready availability of rescue analgesic regimens.

With regard to identification of high-risk patients, a review recommends a number of issues to be considered in the preoperative assessment, as they will increase the risk of poor pain control postoperatively.³⁰ These include a past history of increased preoperative pain (eg, patients with chronic pain) as well as the observation of increased preoperative anxiety. Younger patients and females are also at increased risk. These proposals are supported by data that show preoperative pain to be best predictive factor of postoperative pain.³¹

Finally, the type of surgery is important, as there are now data that certain operations including appendectomy, cholecystectomy, hemorrhoidectomy, and tonsillectomy as well as longer lasting operations lead to more postsurgical pain. The latter point is in line with increasing interest in procedurespecific pain management;³² such evidence-based, procedurespecific guidelines for a number of operations are available at the PROSPECT website (http://www.postoppain.org). An example from the ambulatory setting would be adenoidectomy and adenotonsillectomy, two common day-case procedures done in children, which frequently cause significant postoperative pain. Following adenoidectomy, acetaminophen may suffice, whereas adenotonsillectomy causes significantly more pain requiring at least a combination of acetaminophen with a nonsteroidal anti-inflammatory drug (NSAID).33 Last, but not least, failure of a specific analgesic regimen requires rapid implementation of a rescue strategy.³⁰

The importance of evidence-based, multimodal analgesic regimens extending longer into the postoperative period has been highlighted in recent literature, and it is suggested that more future studies on this topic should be undertaken.³⁴

Concept of multimodal analgesia

Multimodal or balanced analgesia, a concept developed around 20 years ago,³⁵ has become the something of a gold standard for postoperative pain management. Underpinning this concept has been the idea to use more than one analgesic compound or modality of pain control. Combinations of different medications with different mechanisms of action and/or working at different sites along the pain pathway are used to obtain additive (or even synergistic) pain relief, while leading to an opioid-sparing effect and thereby minimizing adverse effects.

The concept of multimodal analgesia is now widely supported by the literature and in recent guidelines.^{23,30} The new practice guidelines for acute pain management in the perioperative setting by the American Society of Anesthesiologists' Task Force on Acute Pain Management state specifically that, whenever possible, anesthesiologists should use multimodal pain management therapy including regional blocks and an around-the-clock regimen of Cox-2 Inhibitors (coxibs) or nonselective NSAIDs and/or acetaminophen.36 Such multimodal analgesia with an emphasis on nonopioids and local anesthetics is a promising concept. This is true in particular after ambulatory surgery, where classical adverse effects of opioids such as nausea and vomiting can delay discharge and increase readmission rates.37 In the setting of ambulatory surgery, after incomplete pain relief as discussed above, adverse effects of opioids are the second most common cause for readmission of patients.³⁸ A good example of the benefits of even avoiding weak opioids such as codeine by combining nonopioids (acetaminophen and ibuprofen) is a trial in which patients in the nonopioid group were more satisfied with their analgesia and had fewer side effects.39

Combinations for which benefits along the concept of multimodal analgesia have been identified include acetaminophen, NSAIDs and coxibs, alpha-2-delta modulators (gabapentin and pregabalin), *N*-methyl-D-aspartate (NMDA) receptor antagonists (ketamine), alpha-2 receptor agonists (such as clonidine and dexmedetomidine), and local anesthetics.⁴⁰

Analgesics Nonopioid analgesics

Acetaminophen, nonselective NSAIDs, and COX-2 selective NSAIDs (coxibs) have become the mainstay of the background analgesia in a multimodal analgesia approach to postoperative pain in all surgical settings.⁴¹

Acetaminophen is obviously the weakest of the nonopioid analgesics.⁴² However, it has also a very low rate of adverse effects, as long as used in therapeutic doses <4 g/day, and nearly no contraindications.⁴³ It is therefore not surprising that it is the most commonly used background analgesic in multimodal approaches. In a survey of analgesia after ambulatory surgery in Sweden, it was used in 95% of cases.² There are even minor surgical interventions performed in an ambulatory setting where acetaminophen may be a sufficient analgesic on its own; in a study, 82% of patients in such a setting were satisfied or very satisfied with acetaminophen as their only analgesic.⁴⁴ This study used intravenous acetaminophen, which is more costly than oral administration, but may be particularly useful for perioperative administration. In an interesting metaanalysis, perioperative intravenous acetaminophen (best given before surgery) resulted in significant reduction of PONV. Finally, acetaminophen can be combined with NSAIDs, and this combination provides analgesia superior to each single drug.⁴⁵ This is the simplest form of multimodal analgesia and has been specifically demonstrated for the combination of acetaminophen with ibuprofen.⁴⁶

Nonselective NSAIDs and coxibs are significantly more effective than acetaminophen with much lower numbers-needed-to-treat (NNTs) in the range 1.7–2.7.⁴² There are no differences in efficacy between NSAIDs and coxibs here. The role of these nonopioids as a component of multimodal analgesia is well established, with clear demonstration of improved analgesia, reduced opioid requirements, and, thereby, reduced adverse effects such as nausea, vomiting, and sedation.⁴⁷ The use of ibuprofen (120 mg/day) or celecoxib (400 mg/day) for 4 days after ambulatory surgery reduced the need for breakthrough analgesia in the early post-discharge period, leading to improved patient satisfaction and quality of recovery.⁴⁸ Whenever they are not contraindicated, these drugs should be a component of any multimodal analgesic regimen in the ambulatory setting.

However, adverse effects limit the use of NSAIDs in particular. Coxibs with their reduced adverse event profile offer an advantage here; their benefits include reduced gastrointestinal ulceration, lack of platelet inhibition with reduced perioperative blood loss, and lack of induction of bronchospasm in patients with aspirin-exacerbated respiratory disease.49 The advantages of coxibs with regard to reduced gastrointestinal ulceration do not only become obvious in the chronic setting, but they are even superior to NSAIDs when combined with a proton pump inhibitor.⁵⁰ Even in the acute setting of short-term use (5-7 days), NSAIDs such as ketorolac and naproxen cause gastric ulcerations in 20%-40% of cases, while coxibs have a rate similar to placebo.49 While a number of studies and meta-analyses show an increased risk of postoperative bleeding with perioperative NSAIDs,^{47,51} coxibs show a reduced risk compared to NSAIDs52 and blood loss identical to placebo.53

In countries where available, the intravenously injectable coxib, parecoxib, might be particularly useful, as it permits

perioperative use. The cardiovascular safety of this compound in the perioperative setting has been confirmed in a meta-analysis with no increased risk of cardiovascular events compared to placebo.⁵⁴ After ambulatory laparoscopic cholecystectomy, pre- or intraoperatively administered parecoxib was associated with less pain and analgesic requirements leading to shorter times to attain recovery room and hospital discharge criteria compared to placebo.⁵⁵

The most important safety consideration for the use of any NSAIDs is their effect on renal function. While their short-term use causes only transient reduction in renal function of no relevance in patients with normal renal function,⁵⁶ use in patients with impaired renal function or risk factors such as hypotension/hypovolemia or concomitant use of other nephrotoxic agents increases the risk.

In countries where available, metamizol (dipyrone) is another valuable nonopioid for the ambulatory surgical setting. It is highly effective,⁵⁷ has an additional spasmolytic effect,⁵⁸ and has very little adverse effects with regard to the gastrointestinal, cardiovascular, and renal systems.⁵⁹ There is ongoing debate on the extremely low risk of agranulocytosis, which has resulted in it being registered only in a limited number of countries worldwide.⁵⁹ However, it is recommended and used widely in countries where available, such as The Netherlands, Austria, and Germany.⁴¹

Overall, all nonopioids are a very useful component of multimodal analgesia after ambulatory surgery and can contribute to improved analgesia and reduced opioid side effects through their opioid-sparing effects. The selection of the most suitable nonopioid for a specific patient should be governed by the severity of pain, comorbidities, and, thereby, contraindications and drug availability in the respective setting.⁴¹

Opioid analgesics

Opioids play an important role as analgesics in the immediate perioperative period and as rescue analgesic in ambulatory anesthesia. As mentioned before, multimodal analgesia helps to minimize opioid requirements and thereby opioid related adverse effects such as sedation, nausea, vomiting, and constipation, which may have negative effects on early recovery (affecting discharge from recovery room and from hospital) and resumption of normal activities.³⁷

A specific recent concern has developed based on reports of death or opioid-induced ventilatory impairment (OIVI) after codeine use in children. The risk is linked to genetically predisposed ultrarapid metabolization of codeine to morphine (cytochrome P450 2D6-dependent) and in particular

increased after tonsillectomy and/or adenoidectomy (most commonly performed in an ambulatory setting).⁶⁰ The reason is obviously that children who need this operation often have sleep-disordered breathing; a boxed warning by the FDA on codeine in children after tonsillectomy and adenoidectomy is now in place.⁶¹

Co-analgesics Alpha-2-delta modulators (gabapentin, pregabalin)

In general, gabapentin and pregabalin have become important components of multimodal analgesia. Usually administered as a premedication, they do not only provide preoperative sedation and anxiolysis but have also beneficial effects with regard to improved analgesia, reduced opioid requirements, and thereby reduced adverse effects of opioids, in particular PONV.^{62,63} The reduction of PONV might even be a specific effect of these compounds.⁶⁴ While these benefits have been shown in some specific surgical settings such as after hysterectomy⁶⁵ and lumbar spinal surgery,⁶⁶ specific studies in the ambulatory setting are limited.

These limited studies have given some contradictory results. For minor gynecological surgery, 100 mg pregabalin had no benefit, suggesting that its role may be in more invasive settings.⁶⁷ In contrast, after laparoscopic hysterectomy, 150 mg pregabalin improved analgesia.⁶⁸ Similarly, after ambulatory laparoscopic cholecystectomy, 1200–1600 mg gabapentin resulted in better analgesia than 15 mg meloxicam.⁶⁹ In this study, an interesting result was that a combination of gabapentin and meloxicam was not superior to the single medications, suggesting that it might not always be useful to combine multiple modalities. This seems also to be the case when 800 mg gabapentin did not improve analgesia provided by a brachial plexus block for arthroscopic shoulder surgery;⁷⁰ possibly a nerve block results in such good analgesia that this cannot be improved by gabapentin.

In the day-care setting, there is understandably concern about the sedating effect of these drugs impairing recovery and discharge. In a study specifically looking at this, 300 mg pregabalin as a premedication prior to ambulatory orthopedic surgery reduced preoperative anxiety and opioid requirements without persisting sedation impairing discharge.⁷¹

Overall, gabapentin and pregabalin may provide anxiolysis and improved analgesia in the ambulatory setting and are recommended here;³⁰ they might be of particular benefit after more than minor surgery and further studies in this setting are needed.

Corticosteroids

In general, there is increasing interest in the use of perioperative corticosteroids, most commonly dexamethasone, to reduce PONV originally⁷² but now also with increasing evidence for an analgesic effect.⁷³ The latter meta-analysis identified the following benefits from perioperative dexamethasone use: reduction of postoperative pain, opioid consumption, time to first analgesia, requirements for rescue analgesia, and stay in the post-anesthesia care unit.

As these advantages would be of significant benefit in an ambulatory surgery setting, it is not surprising that similar results were found in this setting, eg, after ambulatory gynecological surgery.⁷⁴ In view of the low risk of adverse effects with a single perioperative dose of dexamethasone (4–10 mg), the use of this compound as a component of multimodal analgesia can be recommended in the ambulatory setting.

Local and regional anesthesia techniques

Local and regional anesthesia techniques are highly recommended as an integral part of multimodal analgesia, eg, in the recent US guidelines.³⁶ These techniques are able to offer specific benefits to patients after ambulatory surgery. The techniques cover simple local anesthetic infiltration via single dose ("single-shot") administration, often combined with adjuvants to continuous peripheral nerve blockade (CPNB), increasingly continued for a period after discharge.⁷⁵

Local and peritoneal infiltration

Simple infiltration and instillation techniques can be quite useful in providing analgesia with minimal adverse effects after ambulatory surgery. Settings where this has been shown to be effective include wound infiltration after hernia repair,⁷⁶ mid-foot infiltration after hallux valgus repair,⁷⁷ and infiltration of trocar sites with local anesthetic after laparoscopic cholecystectomy.⁷⁸ Here, intraperitoneal local anesthetic instillation was also effective, and the combination of both techniques offered further benefits. Intraperitoneal use was also effective after laparoscopic gynecologic surgery.⁷⁹ However, the duration of these effects is limited; maybe this shortcoming can be overcome by use of new slow-release preparations of local anesthetics such as liposomal bupivacaine.^{80,81}

Single-dose peripheral nerve blockade

The benefits of peripheral nerve blocks after ambulatory surgery are not debatable, and many trials in many settings show excellent analgesia with minimal adverse events.⁸²

Classical uses here include ilioinguinal and iliohypogastric nerve blocks for hernia repair in adults⁸³ and children,⁸⁴ paravertebral blocks for breast surgery,⁸⁵ transversus abdominis plane (TAP) blocks after laparoscopic cholecystectomy,⁸⁶ femoral nerve blocks after anterior cruciate ligament repair,⁸⁷ adductor canal block after arthroscopic meniscectomy,⁸⁸ and a range of brachial plexus blocks for shoulder⁸⁹ and hand surgery.⁹⁰ Pelvic plexus block can be used for ambulatory transrectal ultrasound-guided prostate biopsy⁹¹ and paracervical block for cervical dilatation and uterine interventions.⁹²

To extend the duration and quality of analgesia, adjuvants are often added to single-bolus peripheral nerve blocks, as otherwise the limited duration of effect results in development of pain soon after discharge. This has been recommended in particular in the pediatric setting.⁹³ In addition, as local anesthetics impair motor function while providing analgesia, this may impair early ambulation and initiation of physiotherapy. Here, addition of adjuvants such as clonidine, dexamethasone, buphrenorphine, and midazolam may be beneficial.^{94,95}

Such beneficial effects have been well demonstrated with dexamethasone as well, if added to caudal local anesthetic⁹⁶ as local anesthetic for brachial plexus block.⁹⁷ Similar data exist on buprenorphine as an adjuvant to intraoral nerve blocks.⁹⁸ A meta-analysis of studies of ketamine added to caudal local anesthetics in children, of which many were performed in an outpatient setting, showed prolonged analgesia without prolonged motor block;⁹⁹ however, the practical usefulness of this finding is limited in view of concerns about the neurotoxicity of neuraxial ketamine. Similar findings of a meta-analysis exist for clonidine,¹⁰⁰ and there is also a study of dexmedetomidine via the caudal route.¹⁰¹ However, the addition of clonidine to local anesthetics for intravenous regional anesthesia has shown no benefits.¹⁰²

Whenever patients are discharged after ambulatory surgery before local anesthetic effects have worn off, attention needs to be paid to potential injury to the numb area (knives, heat, cigarettes). However, such discharges are routine practice and should actually be encouraged in view of the excellent analgesia on transfer and in the first hours at home. In a large follow-up series, this practice was shown to be safe;¹⁰³ however, patients need to be provided with appropriate information.

Continuous peripheral nerve blockade

Insertion of a catheter while blocking peripheral nerves permits extension of the analgesia by top-up doses or a continuous infusion. While this approach has already become standard practice in in-patient settings,¹⁰⁴ it is now also used increasingly in an ambulatory setting.^{82,105} Patients are commonly sent home with portable pumps providing a continuous infusion via the peripheral nerve catheter, thereby extending the analgesic effect from the maximum 12-16 hours provided by a single bolus nerve block to a number of days postoperatively, if so desired. These techniques are most commonly used after orthopedic surgery¹⁰⁶ and have been used for various blocks, including paravertebral, interscalene, intersternocleidomastoid, infraclavicular, axillary, psoas compartment, femoral, fascia iliaca, sciatic/ Labat's, sciatic/popliteal, and tibial techniques. Compared to patients discharged home with systemic analgesics, patients using these techniques reported significantly reduced opioid requirements leading to fewer opioid-related adverse effects, less sleep disturbance, faster functional rehabilitation, and higher overall satisfaction.^{82,104,105} Similar findings were made in the pediatric setting.¹⁰⁷ Enabling discharge earlier after more complex orthopedic surgery, these techniques have also potential economic advantages.¹⁰⁸

A few examples of such successful usage are a 2-day interscalene infusion at home after shoulder surgery,¹⁰⁹ continuous popliteal sciatic nerve block for foot and ankle surgery,¹¹⁰ and continuous paravertebral block after short-stay mastectomy.¹¹¹ A more detailed analysis of the routine use of continuous interscalene infusions for shoulder surgery in 300 patients revealed a 4% rate of failure of the technique after discharge from recovery room, one patient developing a site infection requiring antibiotic treatment, and no permanent neurological deficits.¹¹² These results are in line with other large case series. Care needs to be taken to reduce the risk of infection.¹¹³

With regard to safety, the discharge of patients with continuous peripheral nerve blocks requires certain precautions, but are then described as safe.⁸² As always, intravascular placement of the catheter needs to be avoided and confirmed. While it is important that patients and carers get detailed instructions about the technique, its potential adverse effects, and the care for the catheter and the insertion site, it is strongly recommended that patients have access by phone to an anesthesiologist for advice 24 hours a day.¹¹⁴ This requirement is confirmed by case series which show that patients call such a service a considerable number of times to get advice on issues such as equipment malfunction, inadequate analgesia, or problems with catheter removal.^{114,115}

Overall, techniques of local and regional analgesia should be used whenever possible; this is not only true in the inpatient but even more so in the ambulatory surgery setting.

The combination of excellent analgesia with minimal systemic adverse effects and significant reduction of opioid requirements makes these techniques ideal after ambulatory surgery.

Nonpharmacological analgesic techniques

Nonpharmacological techniques are so commonly used in the setting of sports injuries, the home, and physiotherapy, but possibly underutilized after ambulatory surgery. One reason may also be that these techniques are not well studied. However, cryoanalgesia,¹¹⁶ transcutaneous electrical nerve stimulation (TENS),¹¹⁷ and acupuncture/acupressure,^{118,119} among others, have been used for acute pain management after ambulatory surgery.

Discharge analgesia after ambulatory surgery

As outlined above, a major problem with ambulatory surgery is that patients experience pain at home hours or days after discharge. This is not only unacceptable from the point of view of the patients' well-being but has also unwanted consequences such as additional presentations at family practitioners, emergency departments, or even readmissions^{12,13} with significant cost and possibly even medicolegal implications.¹¹⁴

Therefore, these patients require careful instruction and supply of sufficient amounts of appropriate analgesics to cover their pain at home, which may even increase when they become more active and start rehabilitation.

Such supply can be provided by prescription or as a discharge analgesia package. $^{\rm 120}$

On the other hand, there are increasing concerns that provision of discharge analgesics, in particular opioids, would lead to increased long-term use of such analgesics.¹²¹ Furthermore, opioids introduced acutely carry other increased risks such as impaired ventilation, in particular when used in obese patients and those with sleep-disordered breathing and/or when combined with benzodiazepines,¹²² and impaired driving ability.¹²³ There are recent additional concerns in view of the high rate of prescription of opioid overdoses in many countries; opioid provided to patients on discharge may be used by others or even sold on the black market. Therefore, such risks including the risk of abuse need to be identified, and prescriptions of discharge opioids need to be governed by some appropriate precautions.¹²³

These arguments are additional support for the use of multimodal analgesia as the preferred analgesic strategy

after ambulatory surgery, with an emphasis on nonopioids and local and regional techniques.

Disclosure

The Anaesthesiology Unit of the University of Western Australia, but none of the authors personally, has received research and travel funding and speaking and consulting honoraria from bioCSL, Bionomics, Eli Lilly, Grunenthal, Janssen, Mundipharma, Pfizer, Phosphagenics and iX Biopharma within the last 2 years.

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